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1 : *Immunol Rev* 1996 Oct;153:47-83

## CD80, CD86 and CD40 provide accessory signals in a multiple-step T-cell activation model.

Van Gool SW, Vandenberghe P, de Boer M, Ceuppens JL

Department of Pathophysiology, Catholic University of Leuven, Belgium.

In this review, a sequential multiple-step model for T-cell activation is proposed. In a series of in vitro studies, highly purified freshly isolated human peripheral blood T lymphocytes were stimulated through the CD28 receptor, with mAb or with natural ligands B7-1 or B7-2, along with TCR stimulation, in the absence of other costimulatory interactions. Ligation of the CD28 receptor, along with stimulation of the TCR, was found to up-regulate pleiotropic in vitro activities, including the secretion of both Th1 and Th2-type cytokines, B-cell help, and the development of cytotoxic activity. This costimulatory action involves CD4+ and CD8+ as well as naive and memory T-cell subsets. The expression of B7-1 and B7-2 on professional APC in situ in both normal and pathological tissues, and its up-regulation on monocytes by GM-CSF and IFN-gamma is consistent with this role. Additional studies have addressed the contribution of interactions between CD28 and B7-1 and B7-2 in T-cell activation initiated by normal un-engineered APC, such as stimulation with recall antigens and primary MLR. Blockade of the interaction between CD28 and B7-1/B7-2 under these conditions failed to completely inhibit T-cell responses or to induce anergy. Complete inhibition and anergy were, however, induced with a combination of CsA, targeting downstream TCR-triggered signalling, as well as anti-B7-1- and anti-B7-2-directed reagents. Interestingly, and in contrast to anti-LFA-1 mAb, the addition of anti-B7-1 or anti-B7-2 reagents could be delayed until at least 48 h after the initiation of T-cell stimulation, indicating a requirement for a late interaction between CD28 and its counter-receptors. Interactions between CD40L on activated T cells and CD40 on APC may serve to sustain, enhance or prolong the presentation of B7-1 or B7-2 on the APC, and thus to prevent anergy induction, or ineffective or abortive T-cell stimulation. Based on these data a sequential multiple-step T-cell activation model is proposed, and novel strategies for immuno-intervention can be designed.

**Publication Types:**

- Review
- Review, academic

**PMID: 9010719, UI: 97163972**

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☐ 1 : *Eur J Immunol* 1996 Mar;26(3):563-70

**Macrophage-T cell interaction in murine salmonellosis:  
selective down-regulation of ICAM-1 and B7 molecules in  
infected macrophages and its probable role in cell-mediated  
immunity.**

**Gupta S, Vohra H, Saha B, Nain CK, Ganguly NK**

Department of Experimental Medicine & Biotechnology, Postgraduate  
Institute of Medical Education & Research, Chandigarh, India.

Vaccine development and understanding of cellular immune modulatory mechanisms in salmonella infections have been impeded due to the paucity of data on antigens capable of eliciting effective immune responses. The present study was done to evaluate the efficacy of five major purified salmonella antigens (porins, pili, flagella, outer membrane proteins and heat shock proteins) in modulating T cell-macrophage interactions which play a central role in resistance to and recovery from infection with several intracellular pathogens, including salmonella. The results showed that the T cells recovered 10 days post-immunization (D10 T cells) from mice immunized with porins and outer membrane proteins showed maximum proliferation in the presence of macrophages incubated with dead bacteria; however, this response was decreased when T cells were co-cultured with live *Salmonella typhimurium*-infected macrophages. Delayed-type hypersensitivity responses, as measured by increased footpad thickness at 24 h, though induced effectively by porins, pili and flagella, were completely abrogated when D10 T cells were pre-incubated with macrophages infected with live bacteria. The phagocytic and bactericidal ability of normal macrophages, when grown in presence of T cell supernatants, was not influenced by the immunizing agents, but T cell supernatants obtained from mice immunized with porins and heat-shock protein triggered increased bactericidal activity. Further, the expression of the co-stimulatory molecules ICAM-1 and B7 increased with increasing bacteria (dead):macrophage ratio, but this expression was down-regulated upon incubation with live bacteria.

PMID: 8605922, UI: 96182286

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☐ 1 : *Cell* 1994 Jan 28;76(2):287-99

**MHC-dependent antigen processing and peptide presentation:  
providing ligands for T lymphocyte activation.**

**Germain RN**

Lymphocyte Biology Section, National Institute of Allergy and Infectious  
Diseases, National Institutes of Health, Bethesda, Maryland 20892.

**Publication Types:**

- Review
- Review, academic

PMID: 8293464, UI: 94123336

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☐ 1 : *Exp Cell Res* (1988 Feb);174(2):481-90

### Characteristics of the beta-glucan receptor of murine macrophages.

Goldman R

Department of Membrane Research, Weizmann Institute of Science,  
Rehovot, Israel.

Phagocytosis of heat-killed yeast (HK-yeast), zymosan, and glucan particles by thioglycollate-elicited mouse peritoneal macrophages (Tg-macrophages) was inhibited by soluble glucan polymers/oligomers. The inhibitory capacity of soluble glucans decreased steeply with the decrease in the degree of polymerization (DP<sub>n</sub>); i.e., the concentration at which 50% inhibition of phagocytosis was attained was 0.23 microgram/ml for glucan 1 (DP<sub>n</sub> 24.8), 0.8 microgram/ml for glucan 2 (DP<sub>n</sub> 21.9), and greater than 40 micrograms/ml for glucan 3 (DP<sub>n</sub> 13.8). The glucan polymers were obtained by partial hydrolysis of glucan particles with formic acid (90%, 95 degrees C, 20 min) and fractionation according to solubility in ethanol water mixtures. A short preincubation (5 min, 4 or 37 degrees C) of Tg-macrophages with glucan 1 led to a subsequent inhibition of HK-yeast phagocytosis. Recovery of the phagocytic function was slow (27% in 3 h; 68% in 5 h) and required protein synthesis. beta-Glucan receptor expression was also suppressed by dexamethasone treatment. Mannan exerted at high concentrations (5 mg/ml) a partial inhibitory activity which was totally abrogated by beta-glucanase treatment. Treatment of macrophages with glucan together with mannan did not enhance the inhibitory capacity of glucan beyond the component abrogated by enzyme treatment. Contribution of local opsonization of HK-yeast to the phagocytic response (involvement of complement receptors) was indirectly negated; (a) glucan 1 which inhibits HK-yeast phagocytosis by up to 95% is not an activator of complement and therefore could not compete for the opsonizing proteins; (b) cycloheximide treatment in itself inhibited only partially HK-yeast phagocytosis whereas it inhibited the reexpression of the glucan receptors; (c) glucan 1 did not affect the phagocytosis of serum opsonized HK-yeast. Thus under the experimental conditions described, phagocytosis of HK-yeast by murine macrophages is mediated by and large by the beta-glucan receptors, while the mannose receptors and complement receptors do not contribute to the process.